INTERNATIONAL SEARCH REPORT

International Application No
PCT/CZ 03/00003

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61L15/28 A61L26/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
WPI Data, EPO-Internal, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	✓DATABASE WPI Section Ch, Week 199910 Derwent Publications Ltd., London, GB; Class A96, AN 1999-114793 XP002245695 & JP 10 338638 A (TOA YAKUHIN KK), 22 December 1998 (1998-12-22) abstract	1-5
A	✓WO 97 02845 A (SQUIBB BRISTOL MYERS CO ;HOLLINGSBEE DEREK (GB); JACQUES ELIZABETH) 30 January 1997 (1997-01-30) claims; examples	1-6
A	✓US 5 442 053 A (DELLA VALLE FRANCESCO ET AL) 15 August 1995 (1995-08-15) claims	1-6

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
27 June 2003	11/07/2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	ESPINOSA, M

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
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Patent document cited in search report	Publication date	Patent family member(s)		Publication date
JP 10338638 A	22-12-1998	NONE		
WO 9702845 A	30-01-1997	AU	6698996 A	10-02-1997
		WO	9702845 A1	30-01-1997
		GB	2319729 A ,B	03-06-1998
US 5442053 A	15-08-1995	IT	1212892 B	30-11-1989
		IT	1178041 B	03-09-1987
		IT	1229075 B	17-07-1991
		US	4593091 A	03-06-1986
		US	5631241 A	20-05-1997
		AR	231992 A1	30-04-1985
		AT	54921 T	15-08-1990
		AU	575861 B2	11-08-1988
		AU	3414884 A	18-04-1985
		BE	900810 A2	11-04-1985
		CA	1205031 A1	27-05-1986
		CH	666897 A5	31-08-1988
		DE	3482812 D1	30-08-1990
		DK	485384 A	12-04-1985
		EP	0138572 A2	24-04-1985
		ES	8507573 A1	16-12-1985
		FI	843990 A ,B,	12-04-1985
		FR	2553099 A1	12-04-1985
		HK	66091 A	30-08-1991
		HU	36834 A2	28-10-1985
		IE	57931 B1	19-05-1993
		IL	73217 A	30-06-1991
		IN	163192 A1	20-08-1988
		JP	2611159 B2	21-05-1997
		JP	8259604 A	08-10-1996
		JP	6008323 B	02-02-1994
		JP	61028503 A	08-02-1986
		KR	8601148 B1	18-08-1986
		LU	85582 A1	04-06-1985
		NO	844054 A ,B,	12-04-1985
		PT	79339 A ,B	01-11-1984
		SG	59491 G	23-08-1991
		US	5166331 A	24-11-1992
		US	5925626 A	20-07-1999
		ZA	8407942 A	29-05-1985
		IL	96943 A	15-03-1993
		NZ	209850 A	27-11-1987
		PH	23149 A	11-05-1989
		AT	98495 T	15-01-1994
		AU	592077 B2	04-01-1990
		AU	5566286 A	16-10-1986
		BE	904547 A1	03-10-1986
		CH	672886 A5	15-01-1990
		DE	3689384 D1	27-01-1994
		DE	3689384 T2	07-07-1994
		DK	149886 A	06-10-1986
		EP	0197718 A2	15-10-1986
		EP	0555898 A2	18-08-1993
		ES	8800055 A1	01-01-1988
		FI	861395 A ,B,	06-10-1986

SUMMARY OF FACTS AND SUBMISSIONS

European patent No. 1 487 506 was granted in response to European patent application No. 03704190.2 filed on 15.01.2003 claiming a priority of CZ 200212746 U of 18.01.2002. The mention of the grant of the patent was published in European Patent Bulletin 2007/14 on 04.04.2007. The patent proprietor is CPN Spol. S.R.O. (hereinafter referred to as the Proprietor). The title of the patent reads "Preparation for wound healing and prevention of bandage adhesion to the wound".

Notice of opposition has been filed on 21.12.2007 by Gedeon Richter Plc. (hereinafter referred to as the Opponent).

The Opponent requested that the opposed patent be revoked as a whole under Article 100(a) EPC on the grounds of lack of inventive step (Article 56 EPC) and under Article 100(b) EPC on the grounds of insufficient disclosure (Article 83 EPC).

The Opponent additionally requested Oral proceedings, should the Opposition division intend to take any other decision.

The following documents were cited by the Opponent in support of his request:

D1 ... EP 0 480 189 A
D2 ... US 5 442 053 A
D3 ... EP 0 413 016 B
D4 ... EP 0475 807 A
D5 ... EP 1 005 874 A
D6 ... EP 0 055 023 A
D7 ... EP 0 221 728 A
D8 ... Brockhaus Enzyklopädie, Band 11, page 201 (1997)
D9 ... JP 10338638 A (abstract)

The Opponent argued in his note of opposition that the opposed patent lacks disclosure, since it contains no indication about how to measure the molecular weight of 200,000 to 2,500,000 of the hyaluronic acid specified in claim 1 as granted.

The Opponent further considered the granted set of claims to lack an inventive step according to Article 56 EPC in view of D3 as the closest prior art. D3 discloses the manufacture of 3d metal complexes/salts of hyaluronic acid, which can be used for wound treatment. Given that iodine in the form of an iodine/potassium iodide complex in aqueous solution (Lugol's iodine) is a widely known antiseptic agent commonly used for the disinfection of wounds, as disclosed e.g., in D6, D7 or D8, it was obvious for the skilled person to incorporate this agent into the composition of D3.

In his letter of reply dated 26.06.2008, the Proprietor requested to reject the opposition and to maintain the patent as granted. He additionally requested Oral proceedings in case the Opposition division does not feel in a position to follow this request.

The Proprietor presented the following evidence in support of his position:

D10 ... R.A. Cooper, Int. Wound J. 4(2), 124-137 (2007)
D11 ... H.D. Dakin, Brit. J. Med. 318-320 (1915)
D12 ... F.C. Kelly, Proc. Royal Soc. Med. 54, 831-836 (1961)
D13 ... H.A. Shelanski et al., J. Internat. Coll. Surgeons 25, 727-734 (1956)
D14 ... Graph 1: % of the encrusted wound as a function of healing time (hours)
D15 ... Fig. 1: Newly developed bandage for wound healing on the polymer basis
D16 ... Graph 2 a-b: weight of the crust (g) and uronic acid (mg) as a function of the healing solution
D17 ... J. Frankova et al., J. Mater. Sci.: Mater. Med. 17, 891-898 (2006)
D18 ... W. Lineaweaver et al., Arch. Surg. 120, 267-270 (1985)
D19 ... Fig. 2 a-d
D20 ... Fig. 3 a-b: Diabetic defect before and after application of Hyiodine
D21 ... Fig. 4 a-b: Post-surgical wounds before and after application of Hyiodine
D22 ... Graph 3: Molecular weight of HA (kDa) as a function of time (hours)
D23 ... Expert opinion from Prof. Ing. Radim Hrdina, CSc., 25.06.2008

The Proprietor stated that the molecular weight indicated in claim 1 of the opposed patent is a weight averaged molecular weight and provided arguments to support his view that the subject-matter of the patent as granted is sufficiently disclosed and involves an inventive step.

With letter of 10.02.2009, the Opponent repeated his objections relating to insufficient disclosure and lack of inventive step and discussed the arguments provided by the Proprietor. The Opponent cited two additional documents:

D24 ... EP 0 487 066 A
D25 ... US 6,015,836 A

and presented new objections relating to inventive step using a combination of any of the documents D1-D3 with D24 or D25 as well as using D24 as the closest prior art.

Following the request of both parties, the Opposition division decided to summon for Oral proceedings in accordance with Article 116(1) EPC.

PRELIMINARY OPINION OF THE OPPOSITION DIVISION

The topics to be discussed during oral proceedings and the provisional opinion of the Opposition division are as follows. It is pointed out, that this opinion is non-binding and may change during the course of the proceedings.

Admissibility of the Opposition

The opposition is admissible, since it meets the requirements of Articles 99(1) and 100 EPC as well as of Rule 76 EPC.

Sufficiency of disclosure

The Opponent argued in his notice of opposition that the invention of the granted patent is not sufficiently disclosed since the molecular weight of the hyaluronic acid of 200,000 to 2,500,000 is indefinite.

The Opposition division considers that the fact that the molecular weight range indicated in claim 1 of the opposed patent can be interpreted in different ways, i.e. as a weight average or number average molecular weight, is a matter of clarity and not of insufficient disclosure.

The interpretation of the molecular weights indicated in claim 1 as weight average or number average molecular weight only determines the choice of one of the starting products. The Opposition division cannot see how this choice would affect the final product in a way that choosing one type of molecular weight would provide the desired result while the other type would not lead to this result.

In view of the indications in the description and the examples, the Opposition division is of the opinion that the opposed patent describes in sufficient detail the preparation of the claimed products that the skilled person would have no difficulties to prepare them. Therefore the requirements of Article 83 EPC are met.

Inventive step

In his notice of opposition, the Opponent chose document D3 as the closest prior art, since this document discloses the use of hyaluronate with the required molecular weight for the

treatment of wounds. In his letter dated 10.02.2009, he then argued that the claimed subject-matter would lack an inventive step in view of any of the documents D1-D3 and D24 as the closest prior art.

The Opposition division considers that document D4 represents the most relevant state of the art for the following reasons:
This document is directed to the provision of wound-covering materials which via a highly aqueous layer assure adequate retention of the exudate and good contact but no adhesion to the wound surface. The highly aqueous layer should not be decomposed or detached when contacted with the wound, thereby facilitating healing of the wound (cf. p. 2, l. 41-46). Therefore, the technical problem underlying D4 is quite similar to the one indicated in the description of the opposed patent. To solve this problem, D4 discloses (cf. claims 1, 6, 8) a wound-covering material comprising a support layer formed of a film of a gel-forming substance such as hyaluronates. The material can further include an antimicrobial agent such as silver.

The subject-matter of claim 1 of the patent in suit differs from D4 in the use of hyaluronic acid with a molecular weight from 200,000 to 2,500,000 instead of hyaluronates and the combination of iodine and potassium iodide instead of silver in D4.

The description of the opposed patent states on column 4, paragraph 22 that the preparation according to the invention actives keratinocytes to produce cytokines in contrary to iodine and potassium iodide separately (an iodine complex) and hyaluronan separately, thereby accelerating wound cleaning and granulation tissue formation. These unexpected effects are not exhibited by either one of the three components of the preparation according to the invention if applied separately.

The Opponent argued in his notice of opposition that the opposed patent merely states that the simultaneous use of hyaluronic acid, iodine and potassium iodide provides an unexpected synergistic effect without providing experimental evidence for it.

Following that objection, the Proprietor filed with his response experimental evidence in form of D14 (Graph 1) showing a shortened healing time and D16 (Graph 2a) showing an increased crust formation when using hyaluronic acid combined with KI_3 compared to hyaluronic acid and KI_3 alone.

The Opposition division concludes from the evidence provided by the Proprietor that the combination of hyaluronic acid, iodine and potassium iodide indeed provides an unexpected synergistic effect.

The objective technical problem underlying the opposed patent is therefore considered to improve the preparation of D4 to accelerate wound cleaning and granulation tissue formation leading to faster wound healing.

D4 already proposes the incorporation of silver as an antimicrobial agent into the wound-covering material and the skilled person was aware of many alternative antimicrobial agents, including the mixture of iodine and potassium iodide. However, faced with the technical problem of accelerating wound cleaning and granulation tissue formation, the skilled person would not have considered incorporating a different antimicrobial agent such as a mixture of iodine and potassium iodide into the wound-covering material of D4, since these agents as such do not have a positive effect on wound healing and the skilled person therefore had no reasonable expectation of success.

The Opponent argued in his letter dated 10.02.2009 that the synergistic effects described in the opposed patent do not justify an inventive step, but are only considered to be bonus effects.

The Opposition division cannot agree to this argument. If for the skilled person the addition of a mixture of iodine and potassium iodide were an obvious possibility in view of the technical problem posed, e.g. to provide an antimicrobial effect, then the synergistic effect could be considered to be a bonus effect, which, despite being unexpected, would not justify an inventive step for the claimed subject-matter.
In the present case, however, the wound-covering material of D1 is already antimicrobial by the presence of silver, so that no need existed to add a further antimicrobial agent.

In view of the submissions by the Opponent, the Opposition division will now consider the choice of the documents D1-D3 as closest prior art for the evaluation of the presence of an inventive step of the claimed subject-matter.

The subject-matter of claim 1 of the granted patent differs from all the documents D1-D3 in the presence of the combination of iodine and potassium iodide instead of the

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Munich, February 10, 2009

Our Ref.: 124 715 n/n12 03704190.2
Opposition against European Patent EP 1 487 506
Opponent: Gedeon Richter Plc.
Patentee: CPN Spol. S R.O.

In response to the patentee's submission dated June 26, 2008.

1. Insufficient Disclosure

As explained in our opposition, the opposed patent suffers from insufficient disclosure, since it is not specified to which kind of average molecular weight the range of 200,000 to 2,500,000, as required in claim 1 of the opposed patent, relates.

1.1 Documents 1 to 30 cited by the patentee

In response, the patentee alleges in Item 1 of his letter that the skilled person knows that the molecular weight is a weight average molecular weight, and cites 30 documents labelled "1" to "30" for support.

Among those documents, 15 documents specify weight average molecular weights, but there is also one document specifying a number average molecular weight. The remaining documents are

|1 nicht Patentanwalt/not German Patent Attorney
|2 nicht/not European Patent Attorney
|3 nicht/not European Trademark Attorney
|4 Dutch Patent Attorney
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silent about this aspect and thus cannot be taken into consideration. As an aside, we note that most of the documents are dated after the priority date of January 18, 2002.

As a conclusion, documents 1-30 do not provide evidence for a common understanding that "molecular weight" could only mean weight average molecular weight. Rather, the patentee himself has submitted a document proving the contrary.

1.2 Patentee's argument relating to the irrelevance of the distinction between number and weight average molecular weight

In addition, the patentee states that even if the claimed range is interpreted as number averaged molecular weight, the invention would be workable, and that the difference between weight- and number average molecular weight is of minor importance.

This argument supposedly means that the claimed range may apply to both the weight and the number average molecular weight, so that the feature is supposed to be met if at least one of the weight or number average molecular weight is within the range. This interpretation, however, is not supported by the disclosure of the opposed patent, and therefore has to be rejected; neither claim 1 nor the description contain any hints whether the numerical range of 200,000 to 2,500,000 relates to the weight and/or the number average molecular weight or, as suggested by the patentee, to at least one of weight or number average molecular weight.

1.3 Insufficiency of the disclosure

Furthermore, the patentee cites Enclosure XIV as support that the claimed preparation can be prepared by a skilled person according to the disclosure in the opposed patent. This evidence, however, is beside the point. Rather, the key issue is whether the skilled person is put in the position of being able to carry out the invention in all its essential aspects and of knowing when he is working within the forbidden area of the claims (see decision T 256/87).

The question whether the skilled person works within the forbidden area, however, depends on whether the numerical range relates to a weight- or number average molecular weight. When working with a hyaluronate with a Mw value of above 2,500,000 and a Mn value below, the skilled person cannot be sure whether he works inside or outside the area of the

claims. This also applies for a hyaluronate with a Mn value below 200,000 and a Mw value above. In both cases, one of the values is inside whereas the other one is outside the forbidden area.

The documents 1-30 as filed by the patentee cannot clarify this aspect, and the patentee's interpretation that the numerical range may apply to at least one of weight or number average molecular weight is not supported by the description. Therefore, neither of the patentee's arguments could establish sufficiency of disclosure.

2 Lack of Inventive Step of the Subject Matter of Claim 1

Furthermore, the subject matter of the opposed patent lacks inventive step, since use of hyaluronate in combination with a disinfectant is well known in the art, and KI/I_2 is a well known disinfectant.

2.1 KI/I_2 formulations

In his response, the patentee argues that at the priority date of the present application, the use of KI/I_2 for the treatment of wounds is so uncommon that the skilled person would not have taken it into consideration. For support, various articles (Enclosures I-IV) relating to the history of iodine disinfectants for wounds are cited. In summary, these articles state that KI/I_2 (Lugol's solution) has disadvantages and has been replaced by safer preparations such as iodoform or polyvinylpyrrolidone iodine. In Enclosure I (see box on page 125), it is, for example, said that Lugol's solution causes acute pain, irritation and stains.

These articles and arguments, however, relate to disinfectants containing KI/I_2 as such, but not to KI/I_2 in combination with suitable excipients for reducing the above disadvantages; such combinations are also widely known in the art. In this respect, the following documents are cited:

D10 EP 0 487 066
D11 US 6,015,836

D10 (claim 1, examples) relates to a disinfectant composition having excellent bactericidal activity, which comprises KI and I_2 in combination with a polysaccharide (HPC) in an

aqueous solution. On page 3, lines 30-33, D10 states that, owing to the HPC, this combination leads to alleviated skin irritation. Furthermore, p.2, lines 8-9 of D10 also suggest application to wounded sited.

Similarly, D11 (claim 1) describes an aqueous KI/I_2 formulation for de-germing of skin, which further comprises a dual chain quaternary ammonium salt. Column 4, lines 22-32 of D11 state that this formulation is non-staining, non-sensitizing and less irritating than phenolic disinfectants, and that it may be used on mucous membranes or skin.

As a result, D10 and D11 show that KI/I_2 formulations are still used as disinfectants for application to the skin, which also may be applied to wounded sites.

2.2 Lack of inventive step in view of any of the documents D1-D3 in combination with D10 or D11.

In view of the teaching of D10 and/or D11, the skilled person starting from any of the documents D1-D3 teaching wound healing compositions comprising hyaluronate in combination with other ingredients, including disinfectants, would not be prevented from using KI/I_2 formulations as the disinfectant. Rather, D10 even suggests the use of the KI/I_2 formulations described therein for the treatment of wounds.

Hence, the claimed subject matter of the opposed patent is obvious in view of the teachings of any of the documents D1-D3 in combination with D10 or D11. We refer to items 4 and 5 of our grounds for opposition for further details.

2.3 Lack of inventive step in view of D10

As D10 discloses an aqueous composition comprising KI/I_2 and a polysaccharide derivative, and also suggests the use thereof for the treatment of wounds, D10 is a further candidate for the closest prior art.

The technical difference between the teaching of D10 and the opposed patent relates to the polysaccharide: The composition of D10 comprises HPC, whereas the composition according to the opposed patent comprises hyaluronate.

Both, HPC and hyaluronate have the effect of complexing and stabilizing the KI/I_2, thus reducing the concentration of free iodine and reducing the irritating effect thereof (see, e.g., page 2, line 44-48 of D10). Hyaluronate, in addition, is known to promote wound healing (see D1-D4).

Hence, when starting from D10 as closest prior art, the objective technical problem to be solved may be seen in the provision of a disinfectant formulation which supports wound healing.

D10 already suggests the use of the formulation for the treatment of wounded sites (see p.2, lines 8-9). Furthermore, as seen from D1-D4, hyaluronate is a well known agent for the treatment of wounded sides, which further supports wound healing. Therefore, it is obvious to the skilled person to add hyaluronate to the formulation of D10, in order to promote wound healing. Hence, the subject matter of claim 1 of the opposed patent is obvious in view of the teaching of D10 in combination with any of the documents D1-D4.

In addition, D10 even teaches that polysaccharide compounds may form complexes with I_2. and/or KI/I_2, reducing the irritant effect thereof. Hence, it is not surprising to the skilled person that hyaluronate, which is a polysaccharide derivative, will have this effect as well. Thus, it is also would be obvious to the skilled person to try replacing the HPC according to D10 with hyaluronate.

2.4 Alleged unexpected effects

According to the patentee, the specific combination of KI/I_2 and hyaluronate exhibits synergistic effects, which are not demonstrated in the specification of the opposed patent itself in detail, but are shown in various subsequent studies (Encloures V to XIII).

These effects, however, do not justify an inventive step. When starting from the hyaluronate according to, e.g., D3 and seeking to improve the disinfectant properties thereof, combination with KI/I_2 is a measure obvious to the skilled person. Vice versa, when starting from the disinfectant composition of D10, which also may be applied to wounds, and seeking to improve the wound healing properties, addition of hyaluronate is obvious.

Further effects of the obvious combination of hyaluronate and KI/I_2 therefore are mere bonus effects, which cannot establish an inventive step.

3. Lack of Inventive Step of the Subject Matter of Claims 2-

The dependent claims of the opposed patent also do not contain any subject matter which might justify an inventive step.

The hyaluronates listed therein are also used in the prior art. D1 and D2 use sodium hyaluronate, and D3 further teaches that zinc hyaluronate has a significantly wound healing activity than sodium hyaluronate. Therefore, the subject matter of claim 2 is obvious in view of D1-D3.

The concentration ranges as specified in claims 3 and 4 also do not involve an inventive step in view of D10; D10 teaches to use up to 0.01 to 1% KI, up to 0.5% I_2, and 0.5 to 10% of the polysaccharide. These ranges correspond to the ranges specified in claims 3 and 4.

Finally, the subject matter of claim 5 is also obvious, since hyaluronates are commonly used in aqueous solutions or aqua-gels, which have to be sterile when used for the treatment of wounds.

4 Summary

Summarizing all of the above, the patentee's evidence did not demonstrate that the numerical range in claim 1 could only refer to a weight average molecular weight. Rather, the patentee himself has cited a document disclosing a number average molecular weight.

Furthermore, the patentee's allegation that the skilled person would not have used KI/I_2 for the treatment of wounds at the priority date of the opposed patent does not hold. On the contrary, D10 and D11 filed herewith are recent documents which show that there are non-irritant aqueous preparations comprising KI/I_2, which are still in use for external application. According to D10, this also includes the treatment of wounds.

The arguments relating to synergistic effects of the combination of KI/I_2 and hyaluronate cannot establish an inventive step, since the combination is as such obvious. Therefore, any further effects (which are not even shown in the opposed patent) are to be regarded as mere bonus effects.

As a conclusion, the request to revoke the opposed patent because of insufficient disclosure and lack of inventive step of the claimed subject matter and the request for oral proceedings in case the Opposition Division does not feel in a position to follow the request are maintained.

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Encl.: D10, D11

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European Patent Office

80298 Munich

Munich, December 21, 2007

Our Ref.: 124 715 n/n12
Opposition against European Patent EP 1 487 506
corresponding to application No. 03704190.2
Opponent: Gedeon Richter Plc.
Patentee: CPN Spol. S R.O.

In the name and on behalf of

Gedeon Richter Plc.
Gyömröi út 19-21
1103 Budapest / HU

an opposition against European Patent EP 1 487 506 B1,

Preparation for wound healing and prevention of bandage adhesion to the wound

held by

CPN Spol. S R.O. 51603 Dolni Dobrouc (CZ)

is filed herewith.

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A draft money order to be charged to our account in the amount of €635 is attached herewith to cover the official opposition fee to be remitted pursuant to Article 99 (1) EPC.

Requests

It is requested that the above-identified patent EP 1 487 506 B1 is revoked in its entirety on the grounds of Article 100 (a) EPC, especially in view of lack of inventive step, and on the grounds of Article 100 (b) EPC.

In case the Opposition Division does not feel in a position to follow the request, oral proceedings in accordance with Article 116(1) EPC are requested.

Grounds of Opposition

1. The Opposed Patent

The subject matter of claim 1 of EP 1 487 506 B1, hereafter named the Opposed Patent, concerns a

(A) preparation for wound healing and prevention of adhesion of the bandage to the wound, characterized by the content of
(B) a physiologically acceptable salt of hyaluronic acid
(C) with a molecular weight of 200,000 to 2,500,000
(D) iodine, and
(E) potassium iodide.

It is noted that feature (C) is indefinite, as there is no specification how the molecular weight is to be measured, and whether the claimed range relates to number averaged or weight averaged molecular weight.

In addition, it is noted that the features (D) and (E) in combination are well known in the art of wound treatment. In fact, aqueous solutions of iodine and potassium iodide (Lugol's solution) are commonly used as an antiseptic or disinfectant (see, e.g., reference D8). The opposed patent states in [0022] that the simultaneous use of hyaluronate and iodine

provides an unexpected synergistic effect leading to faster wound cleaning and healing. However, no experimental evidence was provided by the patentee to show this alleged effect.

Dependent claim 2 specifies the physiologically acceptable salt of hyaluronic acid (A) to be a sodium salt, lithium salt, calcium salt, magnesium salt, zinc salt, cobalt salt, manganese salt or a combination thereof.

Dependent claim 3 defines the amount of the salt of hyaluronic acid to be in the range between 0.05 and 10 wt%, iodine between 0.05 and 2.5 wt% and potassium iodide between 0.05 and 5 wt%.

According to claim 4, depending on claim 3, the amount of both, iodine and potassium iodide, is required to be in the range between 0.075 and 1 wt%.

The subject matter of claim 5 is the preparation according to claim 1 in the form of a sterile aqueous solution or gel.

2. Prior Art

Reference is made to the following documents:

D1 EP 0 480 189 A1
D2 US 5 442 053
D3 EP 0 413 016 B1
D4 EP 0 475 807 A2
D5 EP 1 005 874 A1
D6 EP 0 055 023 A2
D7 EP 0 221 728 A2
D8 Brockhaus Enzyklopädie, Band 11, p. 211 (1997)
D9 JP 10338638 A (abstract)

D1 discloses pharmaceutical compositions for topical use comprising hyaluronic acid sodium salt and a disinfectant selected from the group consisting of cresol derivatives, hexetidine, sulfadiazine silver and sulfadiazine zinc salt for the treatment of sores,

ulcerations and burns (abstract of D1). Consequently, D1 discloses the features (A) and (B) in combination and further teaches to add a disinfectant.

D2 discloses hylauronic acid fractions with 50,000-100,000 Dalton (in the following abbreviated as 50k-100k) molecular weight (Hyalistine), which is primarily used for wound treatment, and with 500k-730k (Hyalectin), which is primarily used for eye surgery (abstract of D2). Column 19, paragraphs 2 and 3, also disclose the use of mixtures of these fractions and of alkali or alkaline earth metal salts thereof. Combination with antimicrobial agents is taught as well (e.g., column 20, line 65). Thus, D2 discloses the combination of features (A), (B) and (C) and further suggests adding an antimicrobial agent.

D3 concerns the manufacture of 3d metal complexes/salts of hyaluronic acid, such as zinc or cobalt hyaluronate (claims 1-3 and 7 of D3). Use for wound treatment is also taught (page 2, line 15). The subject matter of claim 4 of D3 is the combination with additional therapeutic agents. According to the table on page 11, the molecular weight of the hyaluronate is 1850 k. Consequently, D3 discloses the combination of features (A), (B) and (C), and also suggests the addition of other therapeutic ingredients.

D4 discloses a wound covering material comprising two layers (abstract), the lower support layer is in direct contact with the wound and comprises a biocompatible aqueous gel-forming substance (page 2, line 52-53), which may be a hyaluronate (page 3, line 6). Moreover, D4 teaches that such a support layer prevents adhesion to the wound (page 3, lines 37-29) and may comprise an antimicrobial agent (page 4, lines 14-15). Therefore, D4 teaches the combination of features (A) and (B) together with an antimicrobial agent.

D5 discloses hyaluronic acid or alkali metal hyaluronate gels (see [0051] and examples) and medical materials comprising the same (abstract), including adhesion preventing materials for use in surgery ([0072]-[0074], Example 13). These materials may comprise a pharmaceutically active substance ([0073]). The hyaluronic acid according to D5 has a molecular weight of 100-10000 k ([0050]), including the range claimed in the opposed patent. Therefore, D5 discloses the combination of features (A), (B) and (C) and further suggests adding a pharmaceutically active substance.

The subject matter of D6 is an antiseptic adhesive composition for patches or bandages, comprising a pressure sensitive rubber like elastomer, which provides the tackiness of the composition (page 2, line 28), a water soluble hydrocolloid and an antiseptic agent. As

antiseptic agent, the combination of potassium iodide and iodine crystals (features (D) and (E)) may be used, as shown in example 2 (page 6) of D6.

D7 concerns a wound healing composition comprising a monosaccharide and a film forming agent which may be a hydrocolloid (Abstract and page 5, line 34 of D7). Additional use of iodine and of Lugol's solution in particular (page 6, line 9 of D7) is also taught. Thus, D7 discloses the combination of (A), (D) and (E) and further suggests adding an aqua-gel forming ingredient.

Encyclopaedia entry D8 discloses the combination of (D) and (E) as a disinfectant.

D9 (abstract) discloses a preparation for wound healing comprising 0.01-1 % hyaluronate and 0.5-10% povidone iodine. This disclosure corresponds to a combination of features (A), (B) and (D).

In summary, use of compositions and products comprising hyaluronate for wound treatment is known in the art, and also the use in combination with antiseptic agents. These hyaluronates may also have a molecular weight between 200k and 2500k. Therefore, the combination of features (A), (B) and (C) is known in the art. An adhesion preventing effect of hyaluronate gels is also known from D4 and D5.

Moreover, iodine in the form of an iodine/potassium iodide complex in aqueous solution (Lugol's iodine) is a widely known antiseptic agent and is also used for the disinfection of wounds (see, e.g., D6 and D7). Therefore, the combination of features (D) and (E) is also known. D7 even teaches that Lugol's iodine may be used in combination with aqua-gel forming substances for wound treatment, disclosing the combination of features (A), (D) and (E) in combination.

The combination of hyaluronates with iodine is also known in the art, e.g. from D9.

3. Insufficient Disclosure

Feature (C) of the opposed patent is indefinite, as there is no disclosure how the molecular weight is measured, and whether the claimed range applies to a weight average or number average molecular weight. This renders the disclosure of the opposed patent insufficient, as

the skilled person could not determine whether a specific embodiment falls under the scope of the claimed subject matter of the opposed patent or not.

In particular, this applies to the difference between number and weight averaged molecular weight. Since the number average molecular weight is always lower than the weight average molecular weight, hyaluronate fractions with a number averaged molecular weight below 200k can have a weight average molecular weight of above 200k. Vice versa, fractions with a weight average molecular weight of above 2500k can have a number average molecular weight below 2500k. Thus, it depends on the interpretation of the term "molecular weight" whether such an embodiment falls meets feature (C) as claimed in the opposed patent.

In summary, indefinite feature (C) of the opposed patent does not enable the skilled person to determine whether an embodiment falls under the scope of claim 1 or not. According to decision T 256/87 (item 17), the necessary criterion for sufficiency of the disclosure is that that the skilled person reading the specification is put in the position of being able to carry out the invention in all its essential aspects and of knowing when he is working within the forbidden area of the claims. The latter aspect is not met by the disclosure of the opposed patent, as described above, contravening Article 83 EPC.

4. Lack of Inventive Step

Inter alia, document D3 can be considered as closest prior art, since this document discloses the use of hyaluronate with the required molecular weight for the treatment of wounds, as mentioned above. D3 discloses features (A), (B) and (C) in combination, but does not disclose features (D) and (E), though the use of additional therapeutic substances is suggested in claim 4 of D3. According to the teaching of the opposed patent and also D1-D5, the combination of features (A), (B) and (C) is the improvement of wound healing and prevention of adhesion to the wound.

It is well known in the art (see, e.g., D6, D7 and D8) that the technical effect of features (D) and (E) is the disinfection of the wound. Therefore, the objective technical problem to be solved in view of D3 is the provision of a composition for the treatment of wounds with an improved disinfecting effect.

D3 already teaches the combination of the hyaluronate preparations with other therapeutic ingredients, and D1, D2 and D4 even suggest combination with antiseptic or antimicrobial agents. Lugol's iodine is a well-known antiseptic agent commonly used for the disinfection of wounds, as disclosed e.g., in D6, D7 or D8. Moreover, D7 even suggests combining Lugol's iodine with an aqua-gel forming substance for wound treating purposes.

Consequently, it is obvious to the skilled person that the above problem could be solved by the combination with Lugol's iodine. Therefore, the subject matter of claim 1 of the opposed patent does not involve an inventive step in view of D3 in combination with one of the documents D6 to D8 or with the skilled person's medical knowledge and understanding.

In addition, the patentee did not demonstrate any surprising synergistic properties of the claimed composition. Therefore, inventive step also may not be based on unexpected favourable effects.

5 Lack of Inventive Step of the Subject Matter of the Dependent Claims

No inventive merit can also be seen in the subject matter of dependent claims 2-5 of the opposed patent.

As regards claim 2, the claimed hyaluronates are also known from the closest prior art. In particular, D3 discloses zinc, cobalt and manganese hyaluronate, whereas alkali metal hyaluronates such as sodium hyaluronate are the commonly used form, as disclosed, e.g., in D1 or D2. Therefore, the subject matter of claim 2 does not involve an inventive step.

The concentration ratios as claimed in claims 3 and 4 are also obvious, since the specified ranges are very broad and commonly used. In particular, D1 discloses amounts between 0.1-0.5 weight-% of hyaluronate (page 2, line 48 of D1) which is well within the range of 0.05-10% as claimed in the opposed patent, and between 0.1-2% for the disinfectant substance (page 2, line 49 of D1), which is within the ranges for iodine and potassium iodide as defined in claim 3 of the opposed patent and overlaps with the ranges according to claim 4 of the opposed patent.

The subject matter of claim 5 also does not involve an inventive step, since hyaluronates are commonly used in aqueous solutions or aqua-gels, which have of course to be sterile when employed for the treatment of wounds.

6 Summary

In view of the above, it is substantiated to revoke the opposed patent in its entirety since the claimed subject matter suffers from an insufficient disclosure and does not involve an inventive step.

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Encl.: D1-D9